



Clinical trial results:

Neuromuscular Changes In Small For Gestational Age (SGA) Children During Somatropin Therapy - A Prospective Randomized, Controlled, Open-Label Multicenter Trial (SGA-Power Study)

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-004304-39 |
| Trial protocol | DE |
| Global end of trial date | 14 March 2011 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 27 April 2016 |
| First version publication date | 01 July 2015 |
| Version creation reason | • Correction of full data set error resolution |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A6281283 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00625872 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 1 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 1 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

| | |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 06 September 2011 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 March 2011 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

Primary objective was to determine whether growth hormone therapy improved the motor- performance and coordinative skills in pre-pubertal individuals with SGA as defined by efficiency of muscular function.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator:

Treated versus untreated group during 6 month study period.

| | |
|---|--------------|
| Actual start date of recruitment | 01 July 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects**Subjects enrolled per country**

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 23 |
| Worldwide total number of subjects | 23 |
| EEA total number of subjects | 23 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 23 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 23 subjects were enrolled in 5 centres of Germany. Study started from 01 Jul 2008 and completed on 14 Mar 2011.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Somatropin |

Arm description:

Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Somatropin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Somatropin 0.035 milligram/kilogram/day (mg/kg/day) was administered subcutaneously (s.c) according to exact body weight specific calculation for 12 months. Dose adjustments were made at 6 month intervals.

| | |
|------------------|---------|
| Arm title | Control |
|------------------|---------|

Arm description:

No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months.

| | |
|--|---|
| Arm type | Control |
| Investigational medicinal product name | Somatropin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

No treatment for initial 6 months in control group. After 6 months, somatropin 0.067 mg/kg/day was administered s.c. according to exact body weight specific calculation, for the next 12 months.

| Number of subjects in period 1 | Somatropin | Control |
|---------------------------------------|------------|---------|
| Started | 12 | 11 |
| Treated | 12 | 10 |
| Completed | 8 | 5 |
| Not completed | 4 | 6 |
| Consent withdrawn by subject | 1 | - |
| Did not meet entrance criteria | 1 | - |
| Randomized but not treated | - | 1 |
| Study terminated by sponsor | 2 | 5 |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | Somatropin |
| Reporting group description: Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals. | |
| Reporting group title | Control |
| Reporting group description: No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months. | |

| Reporting group values | Somatropin | Control | Total |
|------------------------------------|------------|---------|-------|
| Number of subjects | 12 | 11 | 23 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|------------|--------------|----|
| Age continuous Units: years arithmetic mean standard deviation | 6.6 ± 1 | 7.6 ± 1.4 | - |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 8 | 11 |
| Male | 9 | 3 | 12 |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Somatropin |
| Reporting group description: Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals. | |
| Reporting group title | Control |
| Reporting group description: No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months. | |

Primary: Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6

| | |
|--|---|
| End point title | Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6 |
| End point description: Peak jump power (PJP) was defined as the peak of the calculated power (force multiplied by velocity). It was measured by Leonardo Jumping Platform during two-leg jump. The subject performs 3 jumps and the highest peak (PJP) of the 3 recordings was selected for further calculations. The SDS indicates how similar the subject was to the reference population. Analysis was done on the full analysis set (FAS) population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. | |
| End point type | Primary |
| End point timeframe: Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 ^[1] | 8 ^[2] | | |
| Units: Watt/kilogram (W/kg) | | | | |
| least squares mean (standard error) | -0.15 (± 1.01) | 0.28 (± 0.51) | | |

Notes:

[1] - Number of subjects analyzed (N) signifies the number of subjects evaluable for this outcome measure.

[2] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

| | |
|--|---------------------------------|
| Statistical analysis title | Statistical Analysis at Month 6 |
| Statistical analysis description: Analysis of covariance (ANCOVA) method was used to calculate p-value with treatment, baseline value, study duration and site as covariates. | |
| Comparison groups | Somatropin v Control |

| | |
|---|------------------------------------|
| Number of subjects included in analysis | 12 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.7232 ^[3] |
| Method | ANCOVA |
| Parameter estimate | Least squares (LS) mean difference |
| Point estimate | -0.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.93 |
| upper limit | 3.08 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.1 |

Notes:

[3] - The statistical test was 2-sided and performed at the 5 percent significance level.

Primary: Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6

| | |
|-----------------|---|
| End point title | Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6 |
|-----------------|---|

End point description:

PJP was defined as the peak of the calculated power (force multiplied by velocity). It was measured by Leonardo Jumping Platform during two-leg jump. The subject performs 3 jumps and the highest peak (PJP) of the 3 recordings was selected for further calculations. The SDS indicates how similar the subject was to the reference population. Analysis was done on the per protocol (PP) population- subjects who received the study medication for at least 22 weeks.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 6

| End point values | Somatropin | Control | | |
|-------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 ^[4] | 6 ^[5] | | |
| Units: W/kg | | | | |
| least squares mean (standard error) | -1.02 (± 0.43) | 0.59 (± 0.27) | | |

Notes:

[4] - N signifies the number of subjects evaluable for this outcome measure.

[5] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

| | |
|-----------------------------------|---------------------------------|
| Statistical analysis title | Statistical Analysis at Month 6 |
|-----------------------------------|---------------------------------|

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

| | |
|-------------------|----------------------|
| Comparison groups | Somatropin v Control |
|-------------------|----------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 8 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1941 ^[6] |
| Method | ANCOVA |
| Parameter estimate | LS Mean difference |
| Point estimate | -1.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.04 |
| upper limit | 4.82 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.51 |

Notes:

[6] - The statistical test was 2-sided and performed at the 5 percent significance level.

Primary: Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6

| | |
|-----------------|--|
| End point title | Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6 ^[7] |
|-----------------|--|

End point description:

PJF was defined as the maximum of force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms and as high as possible with the head and chest. It was measured by Leonardo Jumping Platform during two-leg jump. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 6

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses

| End point values | Somatropin | Control | | |
|-------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 ^[8] | 8 ^[9] | | |
| Units: Newtons | | | | |
| least squares mean (standard error) | -0.7 (± 0.62) | -0.55 (± 0.29) | | |

Notes:

[8] - N signifies the number of subjects evaluable for this outcome measure.

[9] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6

| | |
|-----------------|---|
| End point title | Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; Two-leg-jump) in Per Protocol (PP) Population at Month 6 ^[10] |
|-----------------|---|

End point description:

PJF was defined as the maximum of force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms and as high as possible with the head and chest. It was measured by Leonardo Jumping Platform during two-leg jump. The SDS indicates how similar the subject was to the reference population. Analysis was done on the PP population- subjects who received the study medication for at least 22 weeks.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 6

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses.

| End point values | Somatropin | Control | | |
|-------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 ^[11] | 6 ^[12] | | |
| Units: Newtons | | | | |
| least squares mean (standard error) | -0.83 (± 1.27) | -0.85 (± 0.73) | | |

Notes:

[11] - N signifies the number of subjects evaluable for this outcome measure.

[12] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6

| | |
|-----------------|---|
| End point title | Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Full Analysis Set (FAS) Population at Month 6 ^[13] |
|-----------------|---|

End point description:

Vmax was measured by Leonardo Jumping Platform during two-leg jump. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 6

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses.

| End point values | Somatropin | Control | | |
|-------------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 ^[14] | 11 | | |
| Units: Meter/second (m/s) | | | | |
| least squares mean (standard error) | 0.01 (± 0.08) | 0.12 (± 0.09) | | |

Notes:

[14] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Per Protocol (PP) Population at Month 6

| | |
|-----------------|---|
| End point title | Change From Baseline in Maximum Jump Velocity (Vmax; Two-leg-jump) in Per Protocol (PP) Population at Month 6 ^[15] |
|-----------------|---|

End point description:

Vmax was measured by Leonardo Jumping Platform during two-leg jump. Analysis was done on the PP population- subjects who received the study medication for at least 22 weeks.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, Month 6

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses

| End point values | Somatropin | Control | | |
|-------------------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 ^[16] | 9 | | |
| Units: m/s | | | | |
| least squares mean (standard error) | 0.01 (± 0.05) | 0.25 (± 0.06) | | |

Notes:

[16] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Month 6

| | |
|-----------------|---|
| End point title | Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Month 6 |
|-----------------|---|

End point description:

K-ABC was assessed in children between 2.5-12.5 years. Comprised of 16 subtests; 10 mental processing (intelligence) and 6 achievement subtests. Achievement subtests: expressive vocabulary, faces&places, arithmetic, riddles, reading/decoding, reading/comprehension. Sixteen subtests were weighted accordingly to form 5 global scales: sequential processing, simultaneous processing, achievement, non-verbal and mental processing composite. Scores were rated as upper extreme [greater than (>) 131], above average (116-130), average (85-115), below average (70-84), lower extreme [less than (<) 69]. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6

| End point values | Somatropin | Control | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Sequential Processing) | 25.7 (± 8.35) | 28.5 (± 8.33) | | |
| Change at Month 6 (Sequential Processing) | 2.6 (± 5.82) | -1.9 (± 4.15) | | |
| Baseline (Simultaneous Processing) | 45.7 (± 7.2) | 49.8 (± 12.74) | | |
| Change at Month 6 (Simultaneous Processing) | -0.1 (± 4.53) | 1.5 (± 4.3) | | |
| Baseline (Achievement) | 300.7 (± 66.83) | 341.8 (± 76.88) | | |
| Change at Month 6 (Achievement) | 32.1 (± 48.79) | 16.7 (± 27.52) | | |
| Baseline (Nonverbal) | 46.2 (± 8.65) | 49.8 (± 13.21) | | |
| Change at Month 6 (Nonverbal) | -1.4 (± 3.78) | 0 (± 5.35) | | |
| Baseline (Mental Processing Composite) | 70 (± 12.38) | 78.1 (± 19.95) | | |
| Change at Month 6 (Mental Processing Composite) | 1.4 (± 6.39) | -0.9 (± 7.28) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis for Sequential Processing |
|---|--|
| Statistical analysis description: For K-ABC Test (Sequential Processing): Kruskal-Wallis Analysis of Variance (ANOVA) model was used to calculate p-value. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0532 ^[17] |
| Method | Kruskal-wallis |

Notes:

[17] - The statistical test was 2-sided and performed at the 5 percent significance level.

| Statistical analysis title | Statistical Analysis for Simultaneous Processing |
|--|--|
| Statistical analysis description: For K-ABC Test (Simultaneous Processing): Kruskal-Wallis ANOVA model was used to calculate p-value. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3383 ^[18] |
| Method | Kruskal-wallis |

Notes:

[18] - The statistical test was 2-sided and performed at the 5 percent significance level.

| Statistical analysis title | Statistical Analysis for Achievement |
|----------------------------|--------------------------------------|
|----------------------------|--------------------------------------|

Statistical analysis description:

For K-ABC Test (Achievement): Kruskal-Wallis ANOVA model was used to calculate p-value.

| | |
|---|-------------------------|
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.683 ^[19] |
| Method | Kruskal-wallis |

Notes:

[19] - The statistical test was 2-sided and performed at the 5 percent significance level.

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | Statistical Analysis for Non-Verbal |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

For K-ABC Test (Non-Verbal): Kruskal-Wallis ANOVA model was used to calculate p-value.

| | |
|---|--------------------------|
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4935 ^[20] |
| Method | Kruskal-wallis |

Notes:

[20] - The statistical test was 2-sided and performed at the 5 percent significance level.

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical Analysis for Mental Processing |
|-----------------------------------|--|

Statistical analysis description:

For K-ABC Test (Mental Processing Composite): Kruskal-Wallis ANOVA model was used to calculate p-value.

| | |
|---|--------------------------|
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3458 ^[21] |
| Method | Kruskal-wallis |

Notes:

[21] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Months 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in Intellectual Performance of Children Using Kaufmann-Assessment Battery for Children (K-ABC) Test Global Scales at Months 12 and 18 |
|-----------------|--|

End point description:

K-ABC was assessed in children between 2.5-12.5 years. Comprised of 16 subtests; 10 mental processing (intelligence) and 6 achievement subtests. Achievement subtests: expressive vocabulary, faces&places, arithmetic, riddles, reading/decoding, reading/comprehension. Sixteen subtests were weighted accordingly to form 5 global scales: sequential processing, simultaneous processing, achievement, non-verbal and mental processing composite. Scores were rated as upper extreme [greater than (>) 131], above average (116-130), average (85-115), below average (70-84), lower extreme [less than (<) 69].

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[22] | 0 ^[23] | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[22] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[23] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Month 6

| | |
|-----------------|---|
| End point title | Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Month 6 |
|-----------------|---|

End point description:

The KITAP is a computer aided standardized neuro-cognitive development test which allows examination of a wide range of attention and executive functions such as shift of attention (Distractibility); simple reaction time (Alertness); "Sustained Attention", change of reaction (Flexibility); "Divided Attention", controlled reaction disposition (Go/No go) and "Vigilance". It has been designed appropriately for children between the age of 6 to 10 years to allow optimal motivation during testing and to increase validity of results. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. Here, 'n' signifies subjects who received the study drug and evaluated at the time point for each group respectively.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6

| End point values | Somatropin | Control | | |
|--|-------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[24] | 11 | | |
| Units: Seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Distractibility) | 554.3 (± 201.08) | 514.5 (± 127.41) | | |
| Change at 6 Month (Distractibility) (n= 7, 10) | 5.6 (± 230.95) | -11.4 (± 139.52) | | |
| Baseline (Alertness) | 433.9 (± 140.74) | 384.6 (± 124.94) | | |
| Change at 6 Month (Alertness) (n= 8, 10) | -16.1 (± 80.85) | 4 (± 107.42) | | |
| Baseline (Flexibility) | 1350 (± 470) | 1313 (± 477.19) | | |

| | | | | |
|--|------------------|------------------|--|--|
| Change at 6 Month (Flexibility) (n= 8, 10) | -192 (± 492.73) | -211 (± 589.41) | | |
| Baseline (Go/No Go) | 539.8 (± 106.73) | 514.9 (± 91.95) | | |
| Change at 6 Month (Go/No Go) (n= 8, 9) | 35.6 (± 113.38) | -50.2 (± 69.9) | | |
| Baseline (Vigilance) | 822.2 (± 200.65) | 693.4 (± 118.01) | | |
| Change at 6 Month (Vigilance) (n= 7, 10) | -146 (± 278.6) | -31.2 (± 107.62) | | |

Notes:

[24] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

| Statistical analysis title | Statistical Analysis for Distractibility |
|--|--|
| Statistical analysis description: For KITAP Test (Distractibility): Kruskal-Wallis ANOVA model was used to calculate p-value. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6256 |
| Method | Kruskal-wallis |

| Statistical analysis title | Statistical Analysis for Alertness |
|--|------------------------------------|
| Statistical analysis description: For KITAP Test (Alertness): Kruskal-Wallis ANOVA model was used to calculate p-value. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.859 |
| Method | Kruskal-wallis |

| Statistical analysis title | Statistical Analysis for Flexibility |
|--|--------------------------------------|
| Statistical analysis description: For KITAP Test (Flexibility): Kruskal-Wallis ANOVA model was used to calculate p-value. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 |
| Method | Kruskal-wallis |

| | |
|---|-----------------------------------|
| Statistical analysis title | Statistical Analysis for Go/No Go |
| Statistical analysis description: For KITAP Test (Go/No Go): Kruskal-Wallis ANOVA model was used to calculate p-value. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1234 |
| Method | Kruskal-wallis |

| | |
|--|------------------------------------|
| Statistical analysis title | Statistical Analysis for Vigilance |
| Statistical analysis description: For KITAP Test (Vigilance): Kruskal-Wallis ANOVA model was used to calculate p-value. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3291 |
| Method | Kruskal-wallis |

Secondary: Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Months 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in Intellectual Performance of Children Using Kinderversion Der Testbatterie Zur Aufmerksamkeitsprüfung für Kinder (KITAP) Test at Months 12 and 18 |
|-----------------|--|

End point description:

The KITAP is a computer aided standardized neuro-cognitive development test which allows examination of a wide range of attention and executive functions such as shift of attention (Distractibility); simple reaction time (Alertness); "Sustained Attention", change of reaction (Flexibility); "Divided Attention", controlled reaction disposition (Go/No go) and "Vigilance". It has been designed appropriately for children between the age of 6 to 10 years to allow optimal motivation during testing and to increase validity of results.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[25] | 0 ^[26] | | |
| Units: Seconds | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[25] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[26] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Month 6

| | |
|-----------------|---|
| End point title | Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Month 6 |
|-----------------|---|

End point description:

NVLT was assessed for visual memorization that was difficult to verbalize. Test recorded instability index, T-scores (sum of differences of correct {C} - incorrect {IC} "Yes" answers [1]; sum of C "Yes" answers [2]; sum of IC "Yes" answers [3]; sum of differences of C-IC "Yes" answers with high associative items {87%-95%} [4]; sum of differences of C-IC "Yes" answers with low associative items {54%-64%} [5]; difference between difference values for high and low associative items [6]). Scores were rated as below average (<40), average (40-60), above average (>60) and working time ranging between 9-12 minutes. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6

| End point values | Somatropin | Control | | |
|---------------------------------------|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[27] | 11 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Instability Index) | 0.3 (± 0.15) | 0.2 (± 0.21) | | |
| Change at Month 6 (Instability Index) | -0.1 (± 0.11) | -0.1 (± 0.2) | | |
| Baseline (Working Time) | 227 (± 44.27) | 218.3 (± 76.89) | | |
| Change at Month 6 (Working Time) | 10.6 (± 92.95) | -11.1 (± 34.86) | | |
| Baseline [T-scores (1)] | 39.9 (± 13.6) | 43.9 (± 16.53) | | |
| Change at Month 6 [T-scores (1)] | 4.4 (± 11.64) | 6.7 (± 12.12) | | |
| Baseline [T-scores (2)] | 41.6 (± 12.97) | 46.8 (± 14.4) | | |
| Change at Month 6 [T-scores (2)] | 5 (± 10.72) | -0.6 (± 5.5) | | |
| Baseline [T-scores (3)] | 45.9 (± 14.89) | 48.1 (± 18.2) | | |
| Change at Month 6 [T-scores (3)] | 1.5 (± 5.15) | 8.3 (± 12.24) | | |
| Baseline [T-scores (4)] | 39.3 (± 16.97) | 46.4 (± 16.03) | | |
| Change at Month 6 [T-scores (4)] | 5.6 (± 15.53) | 1.4 (± 11.75) | | |
| Baseline [T-scores (5)] | 43.3 (± 11.12) | 43.6 (± 15.13) | | |
| Change at Month 6 [T-scores (5)] | 2.6 (± 9.83) | 7.7 (± 12.59) | | |
| Baseline [T-scores (6)] | 44.9 (± 15.83) | 52.9 (± 19.96) | | |
| Change at Month 6 [T-scores (6)] | 0.9 (± 16.55) | -7.4 (± 14.88) | | |
| Baseline [Age-corrected T-scores (1)] | 33.4 (± 12.18) | 38.6 (± 13.43) | | |

| | | | | |
|--|----------------|----------------|--|--|
| Change at Month 6 [Age-corrected T-scores (1)] | 6 (± 10.21) | 5.2 (± 11.26) | | |
| Baseline [Age-corrected T-scores (2)] | 51.3 (± 7.55) | 54.5 (± 8.1) | | |
| Change at Month 6 [Age-corrected T-scores (2)] | 3.1 (± 5.59) | -0.1 (± 3.38) | | |
| Baseline [Age-corrected T-scores (3)] | 40 (± 13.86) | 41.1 (± 16.38) | | |
| Change at Month 6 [Age-corrected T-scores (3)] | 0.6 (± 4.47) | 7.8 (± 12.13) | | |
| Baseline [Age-corrected T-scores (4)] | 37.4 (± 17.01) | 45 (± 15.21) | | |
| Change at Month 6 [Age-corrected T-scores (4)] | 6.3 (± 14.57) | 4.1 (± 10.63) | | |
| Baseline [Age-corrected T-scores (5)] | 35 (± 11.88) | 37.3 (± 13.48) | | |
| Change at Month 6 [Age-corrected T-scores (5)] | 3.3 (± 10.73) | 6.9 (± 12.57) | | |
| Baseline [Age-corrected T-scores (6)] | 50 (± 16.49) | 55.5 (± 16.64) | | |
| Change at Month 6 [Age-corrected T-scores (6)] | 1.5 (± 19.06) | -4.1 (± 13.77) | | |

Notes:

[27] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Months 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in Intellectual Performance of Children Using Non-verbal Learning Test (NVLT) at Months 12 and 18 |
|-----------------|--|

End point description:

NVLT was assessed for visual memorization that was difficult to verbalize. Test recorded instability index, T-scores (sum of differences of correct {C} - incorrect {IC} "Yes" answers [1]; sum of C "Yes" answers [2]; sum of IC "Yes" answers [3]; sum of differences of C-IC "Yes" answers with high associative items {87%-95%} [4]; sum of differences of C-IC "Yes" answers with low associative items {54%-64%} [5]; difference between difference values for high and low associative items [6]). Scores were rated as below average (<40), average (40-60), above average (>60) and working time ranging between 9-12 minutes.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[28] | 0 ^[29] | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[28] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[29] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Intellectual Performance of Children Using Child Behavior Checklist 4-18 Years (CBCL 4-18) at Months 6, 12 and 18

| | |
|-----------------|---|
| End point title | Change From Baseline in Intellectual Performance of Children Using Child Behavior Checklist 4-18 Years (CBCL 4-18) at Months 6, 12 and 18 |
|-----------------|---|

End point description:

CBCL was standardized for children ages 4 to 18 years and measured child internalizing and externalizing behaviors and total problems. The 4-18 years' checklist contains 140 questions and responses were recorded on a Likert scale: 0 = Not True, 1 = Somewhat or Sometimes True, 2 = Very True or Often True. The range of possible values was 0-280 (0=good to 280=worst).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[30] | 0 ^[31] | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[30] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[31] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; One-leg-jump) at Months 6, 12 and 18

| | |
|-----------------|---|
| End point title | Change From Baseline in Peak Jump Power Standard Deviation Score (PJP-SDS; One-leg-jump) at Months 6, 12 and 18 |
|-----------------|---|

End point description:

PJP was defined as the peak of the calculated power (force multiplied by velocity). It was measured by Leonardo Jumping Platform during one leg jump. The subject performs 3 jumps and the highest peak (PJP) of the 3 recordings was selected for further calculations. The SDS indicates how similar the subject was to the reference population.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[32] | 0 ^[33] | | |
| Units: W/kg | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[32] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[33] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; One-leg-jump) at Months 6, 12 and 18

| | |
|-----------------|---|
| End point title | Change From Baseline in Peak Jump Force Standard Deviation Score (PJF-SDS; One-leg-jump) at Months 6, 12 and 18 |
|-----------------|---|

End point description:

PJF was defined as the maximum of force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms and as high as possible with the head and chest. It was measured by Leonardo Jumping Platform during one leg jump. The SDS indicates how similar the subject was to the reference population.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[34] | 0 ^[35] | | |
| Units: Newtons | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[34] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[35] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximum Jump Velocity (Vmax; One-leg-jump) at Months 6, 12 and 18

| | |
|-----------------|---|
| End point title | Change From Baseline in Maximum Jump Velocity (Vmax; One-leg-jump) at Months 6, 12 and 18 |
|-----------------|---|

End point description:

Vmax was measured by Leonardo Jumping Platform during one leg jump.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[36] | 0 ^[37] | | |
| Units: m/s | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[36] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[37] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test- Peak Jump Power (PJP) at Month 6

| | |
|-----------------|--|
| End point title | Change From Baseline in Five-chair Rising Test- Peak Jump Power (PJP) at Month 6 |
|-----------------|--|

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJP). PJP is defined as the peak of the calculated power (force multiplied by velocity). Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[38] | 9 ^[39] | | |
| Units: kilowatt (kW) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 0.1 (± 0.07) | 0.1 (± 0.05) | | |
| Change at Month 6 | 0 (± 0.07) | 0 (± 0.05) | | |

Notes:

[38] - N signifies the number of subjects evaluable for this outcome measure.

[39] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Peak Jump Power (PJP) at Months 12 and 18

| | |
|---|--|
| End point title | Change From Baseline in Five-chair Rising Test-Peak Jump Power (PJP) at Months 12 and 18 |
| End point description: | |
| The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). PJP is defined as the peak of the calculated power (force multiplied by velocity). | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[40] | 0 ^[41] | | |
| Units: kW | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[40] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[41] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Month 6

| | |
|--|---|
| End point title | Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Month 6 |
| End point description: | |
| The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). PJF is the maximum force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms as high as possible with the head and chest. Analysis was done on the FAS population included- who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[42] | 9 ^[43] | | |
| Units: kilonewton (kN) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 0.4 (± 0.11) | 0.4 (± 0.19) | | |

| | | | | |
|-------------------|-----------------|----------------|--|--|
| Change at Month 6 | 0 (\pm 0.23) | 0 (\pm 0.2) | | |
|-------------------|-----------------|----------------|--|--|

Notes:

[42] - N signifies the number of subjects evaluable for this outcome measure.

[43] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Months 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in Five-chair Rising Test-Peak Jump Force (PJF) at Months 12 and 18 |
|-----------------|--|

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). PJF is the maximum force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms as high as possible with the head and chest.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[44] | 0 ^[45] | | |
| Units: kN | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[44] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[45] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Month 6

| | |
|-----------------|--|
| End point title | Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Month 6 |
|-----------------|--|

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJF). Vmax is defined as the maximum jump velocity. Analysis was done on the FAS population-subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[46] | 9 ^[47] | | |
| Units: m/s | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 0.7 (± 0.22) | 0.6 (± 0.16) | | |
| Change at Month 6 | 0.2 (± 0.29) | 0 (± 0.18) | | |

Notes:

[46] - N signifies the number of subjects evaluable for this outcome measure.

[47] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Months 12 and 18

| | |
|-----------------|---|
| End point title | Change From Baseline in Five-chair Rising Test-Maximum Jump Velocity (Vmax) at Months 12 and 18 |
|-----------------|---|

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: five repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over the chest (time to perform the tasks, maximal PJP, maximal velocity and maximal PJP). Vmax is defined as the maximum jump velocity.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 12 and Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[48] | 0 ^[49] | | |
| Units: m/s | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[48] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[49] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Month 6

| | |
|---|---|
| End point title | Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Month 6 |
| End point description: Chair rising test is performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: 5 repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over chest (time to perform tasks, maximal PJP, maximal velocity and maximal PJF). Time to perform task includes: Average (avg) rise time which is avg time to perform 1 rise, average time per test is the average time to perform 1 test (rise and sitting down) and total time to perform 5 tests. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. | |
| End point type | Secondary |
| End point timeframe: Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|---|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[50] | 9 ^[51] | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (Average rise time) | 1.2 (± 0.9) | 0.7 (± 0.31) | | |
| Change at Month 6 (Average rise time) | -0.5 (± 1.15) | 0.1 (± 0.27) | | |
| Baseline (Average time per test) | 2 (± 0.7) | 2.3 (± 0.6) | | |
| Change at Month 6 (Average time per test) | -0.2 (± 0.54) | -0.1 (± 0.87) | | |
| Baseline (Total time to perform 5 tests) | 9.6 (± 3.91) | 10.8 (± 2.24) | | |
| Change at Month 6 (Total time to perform 5 tests) | 0.1 (± 3.04) | 2 (± 8.48) | | |

Notes:

[50] - N signifies subjects evaluable for the measure.

[51] - N signifies subjects evaluable for the measure.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Months 12 and 18

| | |
|--|--|
| End point title | Change From Baseline in Five-chair Rising Test (Time to Perform the Tasks) at Months 12 and 18 |
| End point description: Chair rising test is performance test (total power output) to measure neuromuscular function of complex movement in standing up. Test allows diagnostics of movement deficits using Leonardo jump plate. Five stand up test: 5 repetitions of rising from a chair on jump plate as quickly as possible with arms crossed over chest (time to perform tasks, maximal PJP, maximal velocity and maximal PJF). Time to perform task includes: Average (avg) rise time which is avg time to perform 1 rise, avg time per test is the avg time to perform 1 test (rise and sitting down) and total time to perform 5 tests. | |
| End point type | Secondary |
| End point timeframe: Baseline, Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[52] | 0 ^[53] | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[52] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[53] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in One-chair Rising Test-Peak Jump Power (PJP) at Months 6, 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in One-chair Rising Test-Peak Jump Power (PJP) at Months 6, 12 and 18 |
|-----------------|--|

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement to stand up. Test allows diagnostics of movement deficits using Leonardo jump plate. One stand up test: rising from a chair on the jump plate as quickly as possible with arms crossed over the chest (analysis of time, PJP, PJF and time of fastest rising). PJP is defined as the peak of the calculated power (force multiplied by velocity).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[54] | 0 ^[55] | | |
| Units: kW | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[54] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[55] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in One-chair Rising Test-Peak Jump Force (PJF) at Months 6, 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in One-chair Rising Test-Peak Jump Force (PJF) at Months 6, 12 and 18 |
|-----------------|--|

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement to stand up. Test allows diagnostics of movement deficits using Leonardo jump plate. One stand up test: rising from a chair on the jump plate as quickly as possible with arms crossed over the chest (analysis of time, PJP, PJF and time of fastest rising). PJF is the maximum force of the ascending part of the jump which the subject performed as a counter-movement jump with freely moving arms as high as possible with the head and chest.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[56] | 0 ^[57] | | |
| Units: kN | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[56] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[57] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in One-chair Rising Test (Time to Perform the Tasks) at Months 6, 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in One-chair Rising Test (Time to Perform the Tasks) at Months 6, 12 and 18 |
|-----------------|--|

End point description:

The Chair rising test is a performance test (total power output) to measure neuromuscular function of complex movement to stand up. Test allows diagnostics of movement deficits using Leonardo jump plate. One stand up test: rising from a chair on the jump plate as quickly as possible with arms crossed over the chest (analysis of time, PJP, PJF and time of fastest rising).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6 , Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[58] | 0 ^[59] | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[58] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[59] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Month 6

| | |
|--|---|
| End point title | Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Month 6 |
| End point description: MIGF was assessed using standard adjustable Jamar dynamometer. MIGF (in Newtons) was calculated by multiplying the dynamometer reading (in kilograms) by a factor of 9.81. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. | |
| End point type | Secondary |
| End point timeframe: Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[60] | 11 | | |
| Units: kg | | | | |
| least squares mean (standard error) | 1.28 (\pm 1.69) | 1.13 (\pm 1.64) | | |

Notes:

[60] - N signifies the number of subjects evaluable for this outcome measure.

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Statistical Analysis at Month 6 |
| Statistical analysis description: ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.956 ^[61] |
| Method | ANCOVA |
| Parameter estimate | LS Mean difference |
| Point estimate | 0.14 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.71 |
| upper limit | 6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.54 |

Notes:

[61] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Months 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in Maximal Isometric Grip Force-Standard Deviation Score (MIGF-SDS) at Months 12 and 18 |
|-----------------|--|

End point description:

MIGF was assessed using standard adjustable Jamar dynamometer. MIGF (in Newtons) was calculated by multiplying the dynamometer reading (in kilograms) by a factor of 9.81. The SDS indicates how similar the subject was to the reference population.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 12, Month 18

| End point values | Somatropin | Control | | |
|-------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[62] | 0 ^[63] | | |
| Units: kg | | | | |
| least squares mean (standard error) | () | () | | |

Notes:

[62] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[63] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Upper Arm Circumference

| | |
|-----------------|------------------------------|
| End point title | Mean Upper Arm Circumference |
|-----------------|------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[64] | 0 ^[65] | | |
| Units: centimeter (cm)] | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[64] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[65] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Thigh Circumference

| | |
|-----------------|--------------------------|
| End point title | Mean Thigh Circumference |
|-----------------|--------------------------|

End point description:

Thigh measurements were taken as a mean of 3 consecutive measurements at upper thigh about an inch down from the crotch line.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[66] | 0 ^[67] | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[66] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[67] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Calf Circumference

| | |
|-----------------|-------------------------|
| End point title | Mean Calf Circumference |
|-----------------|-------------------------|

End point description:

Calf measurements were taken as a mean of 3 consecutive measurements at largest part of calf muscle, usually about 4 inches down from below the knee.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6, Month 12 and Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[68] | 0 ^[69] | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[68] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[69] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height at Month 6

| | |
|--|------------------------|
| End point title | Mean Height at Month 6 |
| End point description: | |
| Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 6 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | 112.8 (± 5.13) | 115 (± 7.93) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height at Months 12 and 18

| | |
|---|---------------------------------|
| End point title | Mean Height at Months 12 and 18 |
| End point description: | |
| Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[70] | 0 ^[71] | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[70] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[71] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity at Month 6

| | |
|--|---------------------------------|
| End point title | Mean Growth Velocity at Month 6 |
| End point description: | |
| Growth velocity measures the annual rate of increase in height. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 6 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | 8.2 (± 1.93) | 4.6 (± 1.44) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity at Months 12 and 18

| | |
|---|--|
| End point title | Mean Growth Velocity at Months 12 and 18 |
| End point description: | |
| Growth velocity measures the annual rate of increase in height. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[72] | 0 ^[73] | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[72] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[73] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height-Standard Deviation Score (SDS) at Month 6

| | |
|-----------------|---|
| End point title | Mean Height-Standard Deviation Score (SDS) at Month 6 |
|-----------------|---|

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 6

| End point values | Somatropin | Control | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | -3.1 (\pm 0.86) | -3.7 (\pm 0.77) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Height-Standard Deviation Score (SDS) at Months 12 and 18

| | |
|-----------------|--|
| End point title | Mean Height-Standard Deviation Score (SDS) at Months 12 and 18 |
|-----------------|--|

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:
Month 12 and Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[74] | 0 ^[75] | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[74] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[75] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity-Standard Deviation Score (SDS) at Month 6

| | |
|-----------------|--|
| End point title | Mean Growth Velocity-Standard Deviation Score (SDS) at Month 6 |
|-----------------|--|

End point description:

Growth velocity measures the annual rate of increase in height. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 6

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | 3.4 (\pm 2.62) | -1.1 (\pm 1.43) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18

| | |
|-----------------|---|
| End point title | Mean Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18 |
|-----------------|---|

End point description:

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[76] | 0 ^[77] | | |
| Units: cm/year | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[76] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[77] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Height-Standard Deviation Score (SDS) at Month 6

| | |
|-----------------|--|
| End point title | Change From Baseline in Height-Standard Deviation Score (SDS) at Month 6 |
|-----------------|--|

End point description:

Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population included subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: cm | | | | |
| least squares mean (standard error) | 0.33 (± 0.21) | -0.22 (± 0.25) | | |

Statistical analyses

| | |
|----------------------------|---------------------------------|
| Statistical analysis title | Statistical Analysis at Month 6 |
|----------------------------|---------------------------------|

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

| | |
|-------------------|----------------------|
| Comparison groups | Somatropin v Control |
|-------------------|----------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1107 ^[78] |
| Method | ANCOVA |
| Parameter estimate | LS Mean difference |
| Point estimate | 0.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.15 |
| upper limit | 1.25 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.31 |

Notes:

[78] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Height-Standard Deviation Score (SDS) at Months 12 and 18

| | |
|--|---|
| End point title | Change From Baseline in Height-Standard Deviation Score (SDS) at Months 12 and 18 |
| End point description: | |
| Standing height was taken as a mean of 3 consecutive measurements using a wall mounted stadiometer. The SDS indicates how similar the subject was to the reference population. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[79] | 0 ^[80] | | |
| Units: cm | | | | |
| least squares mean (standard error) | () | () | | |

Notes:

[79] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[80] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Month 6

| | |
|---|---|
| End point title | Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Month 6 |
| End point description: | |
| Growth velocity measures the annual rate of increase in height. The SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment. | |

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[81] | 9 ^[82] | | |
| Units: cm/year | | | | |
| least squares mean (standard error) | 3.89 (± 1.02) | -0.77 (± 1.4) | | |

Notes:

[81] - N signifies subjects evaluable for the measure.

[82] - N signifies subjects evaluable for the measure.

Statistical analyses

| Statistical analysis title | Statistical Analysis at Month 6 |
|----------------------------|---------------------------------|
|----------------------------|---------------------------------|

Statistical analysis description:

ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates.

| | |
|---|----------------------------|
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 18 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0161 ^[83] |
| Method | ANCOVA |
| Parameter estimate | LS Mean difference |
| Point estimate | 4.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.13 |
| upper limit | 8.21 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.54 |

Notes:

[83] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in Growth Velocity-Standard Deviation Score (SDS) at Months 12 and 18 |
|-----------------|--|

End point description:

Growth velocity measures the annual rate of increase in height. The SDS indicates how similar the subject was to the reference population.

| | |
|------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[84] | 0 ^[85] | | |
| Units: cm/year | | | | |
| least squares mean (standard error) | () | () | | |

Notes:

[84] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[85] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Sitting Height-Standard Deviation Score (SDS)

| | |
|------------------------|--|
| End point title | Sitting Height-Standard Deviation Score (SDS) |
| End point description: | Sitting height was measured using a stadiometer with a specialized chair. The SDS indicates how similar the subject was to the reference population. |
| End point type | Secondary |
| End point timeframe: | Baseline, Month 6, Month 12, Month 18 |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[86] | 0 ^[87] | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[86] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[87] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Body Mass Index-Standard Deviation Score (BMI-SDS)

| | |
|------------------------|--|
| End point title | Body Mass Index-Standard Deviation Score (BMI-SDS) |
| End point description: | The BMI was used to measure body fat based on height and weight. It was calculated by body weight (kg) divided by the height (m) squared. The SDS indicates how similar the subject was to the reference population. |
| End point type | Secondary |

End point timeframe:

Baseline, Month 6, Month 12, Month 18

| End point values | Somatropin | Control | | |
|---|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[88] | 0 ^[89] | | |
| Units: Kilogram per square meter (kg/m ²) | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[88] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[89] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Head Circumference at Months 6, 12 and 18

| | |
|-----------------|---|
| End point title | Change From Baseline in Head Circumference at Months 6, 12 and 18 |
|-----------------|---|

End point description:

The maximum head circumference (usually horizontal just above the eyebrow ridges), was measured from just above the glabella area to the area near the top of the occipital bone (opisthocranium).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Month 6, Month 12, Month 18

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[90] | 0 ^[91] | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[90] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[91] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Head Circumference-Standard Deviation Score (SDS) at Months 6, 12 and 18

| | |
|-----------------|--|
| End point title | Change From Baseline in Head Circumference-Standard Deviation Score (SDS) at Months 6, 12 and 18 |
|-----------------|--|

End point description:

The maximum head circumference (usually horizontal just above the eyebrow ridges), was measured from just above the glabella area to the area near the top of the occipital bone (opisthocranium). The SDS indicates how similar the subject was to the reference population.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 6, Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[92] | 0 ^[93] | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[92] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[93] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Month 6

| | |
|-----------------|--|
| End point title | Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Month 6 |
|-----------------|--|

End point description:

Triceps, supra-iliac and subscapular skinfolds were measured on the right side of the body to the nearest 0.1 mm with a Holtain skinfold caliper. The measurement was performed at the left side of the subject. Triceps skinfold thickness was measured halfway down the left upper arm, while the arm was hanging relaxed at the subject's side. Suprascapular skinfold was measured laterally just below the angle of the left scapula. Suprailiac skinfold was measured just above the iliac crest in the middle-axillary line. SDS indicates how similar the subject was to the reference population. Analysis was done on the FAS population- subjects who received at least 1 dose of study medication and had at least one post baseline efficacy assessment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Month 6 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 11 | | |
| Units: Millimeter (mm) | | | | |
| least squares mean (standard error) | | | | |
| Change at Month 6 (Triceps SDS) | -0.41 (± 0.16) | -0.06 (± 0.18) | | |
| Change at Month 6 (Subscapular SDS) | -0.3 (± 0.1) | -0.16 (± 0.13) | | |
| Change at Month 6 (Suprailiac SDS) | -0.6 (± 0.07) | -0.33 (± 0.12) | | |

Statistical analyses

| | |
|---|--------------------------------------|
| Statistical analysis title | Statistical Analysis for Triceps SDS |
| Statistical analysis description: ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.187 ^[94] |
| Method | ANCOVA |
| Parameter estimate | LS Mean difference |
| Point estimate | -0.35 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.89 |
| upper limit | 0.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.25 |

Notes:

[94] - The statistical test was 2-sided and performed at the 5 percent significance level.

| | |
|---|--|
| Statistical analysis title | Statistical Analysis for Subscapular SDS |
| Statistical analysis description: ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3494 ^[95] |
| Method | ANCOVA |
| Parameter estimate | LS Mean difference |
| Point estimate | -0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.49 |
| upper limit | 0.19 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.15 |

Notes:

[95] - The statistical test was 2-sided and performed at the 5 percent significance level.

| | |
|---|---|
| Statistical analysis title | Statistical Analysis for Suprailiac SDS |
| Statistical analysis description: ANCOVA method was used to calculate p-value with treatment, baseline value, study duration and site as covariates. | |
| Comparison groups | Somatropin v Control |
| Number of subjects included in analysis | 22 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0458 ^[96] |
| Method | ANCOVA |
| Parameter estimate | LS Mean difference |
| Point estimate | -0.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.54 |
| upper limit | -0.01 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.12 |

Notes:

[96] - The statistical test was 2-sided and performed at the 5 percent significance level.

Secondary: Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Months 12 and 18

| | |
|--|---|
| End point title | Change From Baseline in Skinfold Thickness-Standard Deviation Score (SDS) at Months 12 and 18 |
| End point description: Triceps, supra-iliac and subscapular skinfolds were measured on the right side of the body to the nearest 0.1 mm with a Holtain skinfold caliper. The measurement was performed at the left side of the subject. Triceps skinfold thickness was measured halfway down the left upper arm, while the arm was hanging relaxed at the subject's side. Suprascapular skinfold was measured laterally just below the angle of the left scapula. Suprailiac skinfold was measured just above the iliac crest in the middle-axillary line. SDS indicates how similar the subject was to the reference population. | |
| End point type | Secondary |
| End point timeframe: Baseline, Month 12, Month 18 | |

| | | | | |
|-------------------------------------|-------------------|-------------------|--|--|
| End point values | Somatropin | Control | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[97] | 0 ^[98] | | |
| Units: mm | | | | |
| least squares mean (standard error) | () | () | | |

Notes:

[97] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[98] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Bone Density Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

| | |
|-----------------|---|
| End point title | Change From Baseline in Bone Density Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months |
|-----------------|---|

End point description:

Bone Mineral Density (BMD) was measured by pqCT. The Z-score measures the distance of the measured BMD value from the appropriate normal age matched population mean value in units of standard deviation of this population. More negative scores indicate less BMD compared to age matched population and more positive scores indicate higher BMD compared to age matched population.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline, Month 6, Month 12 and Month 18

| End point values | Somatropin | Control | | |
|-------------------------------------|-------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[99] | 0 ^[100] | | |
| Units: z-score | | | | |
| least squares mean (standard error) | () | () | | |

Notes:

[99] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[100] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Bone Structure Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

| | |
|-----------------|---|
| End point title | Change From Baseline in Bone Structure Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months |
|-----------------|---|

End point description:

Bone structure was measured by pqCT. Parameters included: total area, cortical area, marrow area, cortical thickness, cortical density of the radius, bone strength, cross-sectional muscle and fat area, total bone density, bone mineral count, trabecular BMD, bone cross-sectional area. Baseline and post-baseline SDS values transformed to age and sex specific z-score($[\ln(\text{test result}/M)]/S$); Ln=natural logarithm; M=age-/height- and sex-specific mean value; S=age-/height- and sex-specific coefficient of variation). Positive values are above the average for subject's age and sex; negative values are below.

| | |
|---------------------------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Baseline, Month 6, Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[101] | 0 ^[102] | | |
| Units: z-score | | | | |
| least squares mean (standard error) | () | () | | |

Notes:

[101] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[102] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Bone Stability Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months

| | |
|-----------------|---|
| End point title | Change From Baseline in Bone Stability Using Peripheral Quantitative Computed Tomography (pqCT) at 6 or 12 or 18 Months |
|-----------------|---|

End point description:

Bone stability was measured by pqCT. Baseline and post-baseline SDS values transformed to age and sex specific z-score ($\ln(\text{test result}/M)/S$); \ln =natural logarithm; M =age- (or height-) and sex-specific mean value; S =age-(or height-) and sex-specific coefficient of variation) then change from baseline is calculated. Positive values are above the average for subject's age and sex; negative values are below the average.

| | |
|---------------------------------------|---------------------|
| End point type | Other pre-specified |
| End point timeframe: | |
| Baseline, Month 6, Month 12, Month 18 | |

| End point values | Somatropin | Control | | |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[103] | 0 ^[104] | | |
| Units: z-score | | | | |
| least squares mean (standard error) | () | () | | |

Notes:

[103] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

[104] - Data were not analyzed, study was prematurely terminated due to insufficient number of subjects.

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were reported from time of first dose of study treatment up to 28 days after last dose of study treatment.

Adverse event reporting additional description:

EU BR specific adverse event tables were generated separately as per EU format using latest coding.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Control |
|-----------------------|---------|

Reporting group description:

No treatment for initial 6 months in control group. After 6 months, somatropin was administered for next 12 months.

| | |
|-----------------------|------------|
| Reporting group title | Somatropin |
|-----------------------|------------|

Reporting group description:

Somatropin was administered for 12 months. Dose adjustments were made at 6 month intervals.

| Serious adverse events | Control | Somatropin | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 0 / 12 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Control | Somatropin | |
|---|-----------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 11 (63.64%) | 10 / 12 (83.33%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lipoma | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 12 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |

| | | | |
|---|---|---|--|
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 12 (0.00%) 0 | |
| Congenital, familial and genetic disorders Cryptorchism subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 2 / 11 (18.18%) 2 | 2 / 12 (16.67%) 3 | |
| Eye disorders Eyelid oedema subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 | 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 | 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 1 / 12 (8.33%) 1 | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Eczema | 0 / 11 (0.00%) 0 | 1 / 12 (8.33%) 1 | |

| | | | |
|--|---|---|--|
| subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 12 (0.00%) 0 | |
| Renal and urinary disorders Enuresis subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 | 1 / 12 (8.33%) 1 | |
| Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Lordosis subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 1 / 11 (9.09%) 1 | 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 | |
| Infections and infestations Acute tonsillitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Herpes zoster subjects affected / exposed occurrences (all) Lice infestation subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 | 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1 | |

| | | | |
|-----------------------------------|----------------|-----------------|--|
| Otitis media | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 12 (8.33%) | |
| occurrences (all) | 1 | 1 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 2 / 12 (16.67%) | |
| occurrences (all) | 0 | 3 | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 12 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Scarlet fever | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 12 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 11 (0.00%) | 1 / 12 (8.33%) | |
| occurrences (all) | 0 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 1 / 12 (8.33%) | |
| occurrences (all) | 1 | 6 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 11 (9.09%) | 0 / 12 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 23 January 2008 | Changes were requested by the Ethics Committee and the Competent Authorities. Determination of positive effects of growth hormone on bone density, bone structure and enhancement of bone stability were eliminated from the secondary objectives; performance of bone densitometry using pqCT was eliminated from all the visits; measurement of insulin, glucose and glycosylated haemoglobin were changed from optional to obligatory. |
| 04 December 2009 | The primary endpoint was changed from "changes in PJP, PJF and maximal jump velocity after six months" to "efficiency of muscular function after six months"; efficiency of muscular function (Emf) after 12 months, changes in PJP, PJF and maximal jump velocity were added to the secondary endpoints; changes in evaluating attention performance were made due to practicability issues (vigilanz was changed to an optional subtest); measurement of Emf was added to Neuropsychological evaluation. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was prematurely discontinued, therefore not all data was powered.

Notes: